

Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application.

Claim 1. (Currently Amended) A method of modeling or obtaining cardiac tissue ~~or tissue-like structures~~ comprising

(a) differentiating embryonic stem (ES) cells into cardiomyocytes;

(b) ~~co-culturing embryonic stem (ES) cell derived differentiating or differentiated~~ the cardiomyocytes obtained in step (a) with in the presence of differentiating or differentiated fibroblasts and differentiating or differentiated endothelial cells; and

(c) allowing integration and alignment of said differentiating or differentiated the cardiomyocytes[[,]] and fibroblasts and endothelial cells into cardiac tissue or tissue-like structures;

wherein ~~said differentiating or differentiated~~ the cardiomyocytes acquire longitudinal morphology upon integration and alignment with the fibroblasts ~~and endothelial cells;~~ and

wherein said cardiac tissue ~~or tissue-like structures~~ exhibits contractility and cross-striation.

Claim 2. (Previously presented) The method of claim 1, wherein the ES cell of said ES cell-derived cardiomyocyte comprises a selectable marker operably linked to a cardiomyocyte-specific regulatory sequence specific for said cardiomyocyte.

Claim 3. (Original) The method of claim 2, wherein said selectable marker confers resistance to puromycin.

Claim 4. (Previously presented) The method of claim 1, wherein the ES cell of said ES cell-derived cardiomyocyte comprises a reporter gene operably linked to a cardiomyocyte-specific regulatory sequence specific for said cardiomyocyte.

Claim 5. (Previously presented) The method of claim 4, wherein said cardiomyocyte-specific regulatory sequence of the reporter gene is substantially the same as said cardiomyocyte-specific regulatory sequence of the marker gene.

Claim 6. (Original) The method of claim 5, wherein said reporter is selected from different color versions of enhanced green fluorescent protein (EGFP).

Claim 7. (Previously presented) The method of claim 5, wherein said marker gene and said reporter gene are contained in the same recombinant nucleic acid molecule.

Claim 8. (Previously presented) The method of claim 7, wherein said marker gene and said reporter gene are contained in the same cistron.

Claims 9-10. Cancelled.

Claim 11. (Previously presented) The method of claim 2, wherein said cardiomyocyte-specific regulatory sequence is atrial-specific, ventricular-specific, or both atrial and ventricular-specific.

Claims 12-14. Cancelled.

Claim 15. (Currently amended) A co-culture of cardiomyocytes[[,]] and fibroblasts ~~and endothelial cells~~ obtainable by culturing the cardiomyocytes[[,]] and fibroblasts ~~and endothelial cells~~ of claim 1.

Claim 16. (Previously presented) A cardiac tissue obtainable by the method of claim 1.

Claims 17-25. Cancelled.

Claim 26. (Previously presented) The method of claim 8, wherein the promoter is selected from the group consisting of α MHC, MLC2V, catherin, Tie-2 and collagen promoter.

Claims 27-39. Cancelled.

Claim 40. (Currently Amended) The method of claim 1, further comprising analyzing the physiological or developmental status or both of the cardiomyocytes[[,]] and fibroblasts~~and endothelial cells~~.

Claim 41. (Currently Amended) The method of claim 40, wherein the status is analyzed by monitoring the differentiation of electrical activity of the cardiomyocytes[[,]] and fibroblasts~~and endothelial cells~~ on an array.

Claim 42. (Original) The method of claim 41, wherein said status is analyzed by recording the extracellular field potentials with a microelectrode array (MEA).

Claims 43-48. Cancelled.

Claim 49. (Previously presented) The method of claim 1 for analyzing early steps of tissue formation during embryonic development or the influence of factors and compounds on this process.

Claims 50-69. Cancelled.

Claim 70. (Previously presented) The method of claim 1, wherein said one or more cells are genetically engineered to (over)express or inhibit the expression of a target gene.

Claim 71. (Previously presented) The method of claim 1, wherein a compound known to activate or inhibit differentiation process or tissue structure formation or both is added to the culture medium.

Claim 72. (Currently amended) The method of claim 1, wherein the said one ~~or more~~ cells or cardiac tissue are contained in a container.

Claim 73. (Previously presented) The method of claim 72, comprising taking three or more measurements, optionally at different positions within the container.

Claim 74. (Previously presented) The method of claim 72, wherein said container is a well in a microtiter plate.

Claim 75. (Original) The method of claim 74, wherein said microtiter plate is a 24-, 96-, 384- or 1586- well plate.

Claims 76-81. Cancelled.

Claim 82. (New) The method of claim 1, further comprising culturing the cardiomyocytes and fibroblasts in the presence of endothelial cells.

Claim 83. (New) A cardiac tissue obtained by the method of claim 82.

Claim 84. (New) The method of claim 82, further comprising analyzing the physiological or developmental status or both of the cardiomyocytes, fibroblasts, and endothelial cells.

Claim 85. (New) The method of claim 84, wherein the status is analyzed by monitoring the differentiation of electrical activity of the cardiomyocytes, fibroblasts, and endothelial cells on an array.